LUNGENVOLUMENREDUKTION

THERAPIEOPTIONEN BEI FORTGESCHRITTENER COPD

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Kantonsspital Frauenfeld

10. Thurgauer Symposium
3.9.15

COPD «Basistherapie»

Inhalative Therapie* der COPD[1,2]

Therapieempfehlung Patientengruppe A (tiefes Risiko, wenig Symptome)	
Erste Wahl	**Alternative**
SAMA oder **SABA**	**LAMA** oder **LABA** oder **SAMA + SABA**

Therapieempfehlung Patientengruppe B (tiefes Risiko, viele Symptome)	
Erste Wahl	**Alternative**
LAMA oder **LABA**	**LAMA + LABA**

Therapieempfehlung Patientengruppe C (hohes Risiko, wenig Symptome)	
Erste Wahl	**Alternative**
0-1 Exazerbationen pro Jahr	
LAMA	**LAMA + LABA**
≥2 Exazerbationen pro Jahr	
ICS + LABA	

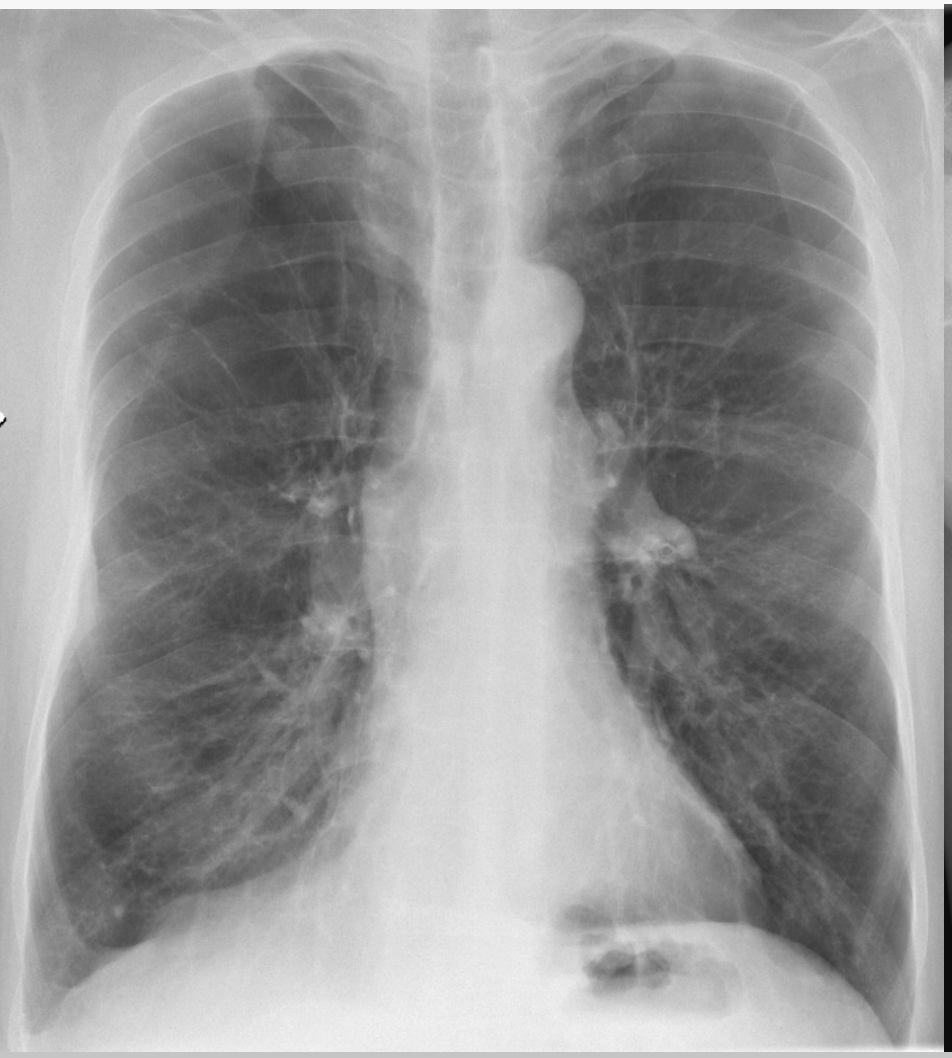
Therapieempfehlung Patientengruppe D (hohes Risiko, viele Symptome)	
Erste Wahl	**Alternative**
0-1 Exazerbationen pro Jahr	
LAMA	**LAMA + LABA**
≥2 Exazerbationen pro Jahr	
ICS + LABA oder **ICS + LABA + LAMA**	**LAMA + LABA + ICS**

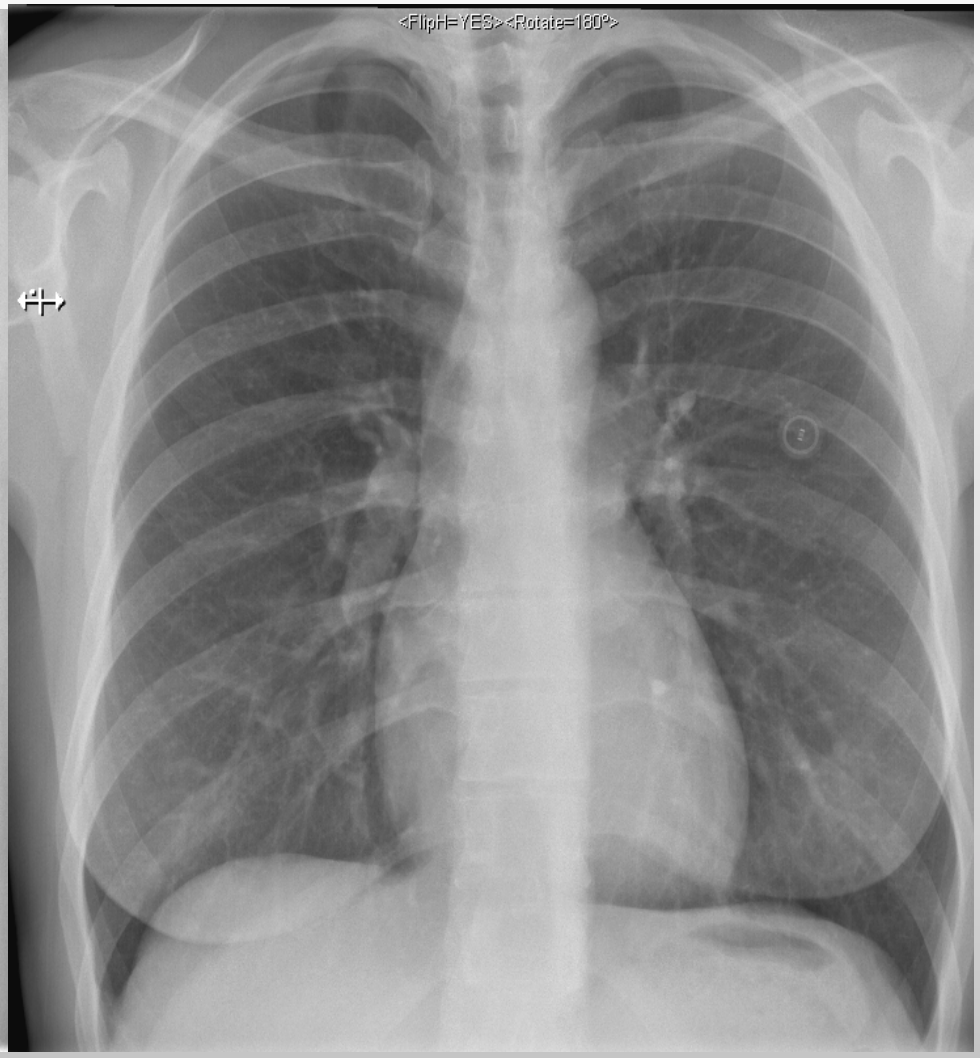
Nicht-medikamentöse Therapie: Rauchstopp, Grippeimpfung, körperliche Aktivität, Patientenschulung

SAMA	Kurzwirksames Anticholinergikum	LABA	Langwirksamer $ß_2$-Agonist, z.B. Onbrez® Breezhaler®
SABA	Kurzwirksamer $ß_2$-Agonist	LAMA + LABA	Duale Bronchodilatation, z.B. Ultibro® Breezhaler®
LAMA	Langwirksames Anticholinergikum, z.B. Seebri® Breezhaler®	ICS	Inhalatives Steroid
		ICS + LABA	Inhalatives Steroid und langwirksamer $ß_2$-Agonist

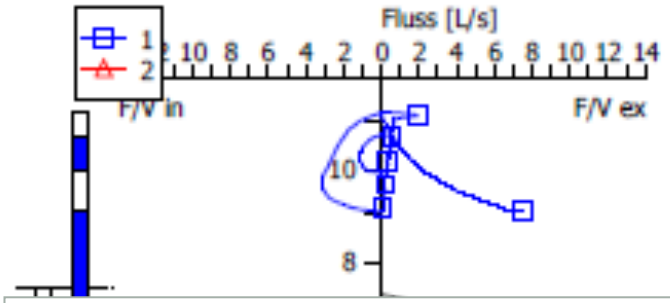
*Für weitere Therapieempfehlungen wie z.B. PDE-4 Hemmer sind die GOLD-Empfehlungen zu konsultieren auf www.goldcopd.org.

COPD Pathophysiologie





Lungenfunktion Gesamtreport Vor / Nach



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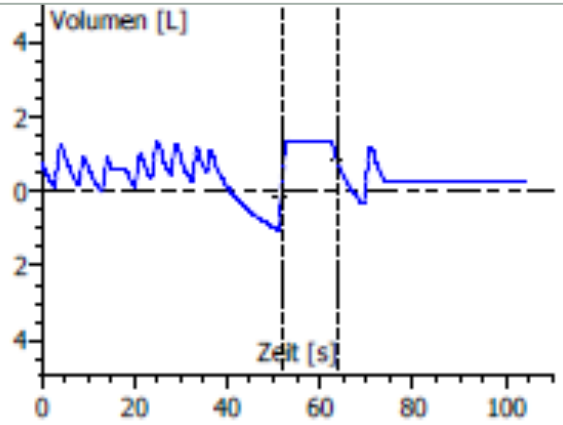
Volumina:

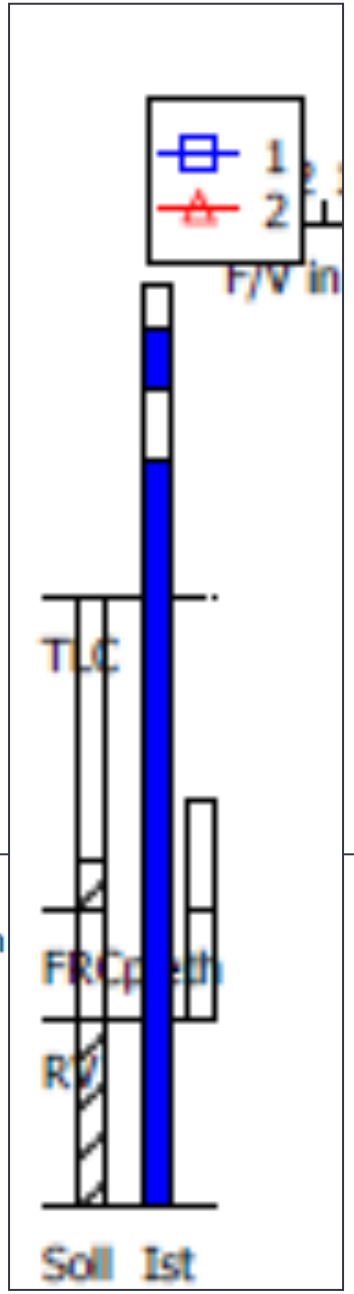
		Soll	Vor	%V/S	Nach
VC MAX	[L]	4.94	2.14	43.4	2.63
ERV	[L]	1.31	0.88	67.3	
IRV	[L]		0.51		
IC	[L]	3.63	1.26	34.7	

Bodyplethysmographische Volumina:

		Soll	Vor	%V/S
TLC	[L]	7.46	11.28	151.2
FRCpleth	[L]	3.65	10.02	274.2
RV	[L]	2.34	9.14	390.2
RV % TLC	[%]	35.02	81.01	231.3



		Soll	Vor	%V/S	Nach
DLCO SB	[mmol/min/kPa]	10.63	1.94	18.2	
DLCO/VA	[mmol/min/kPa/L]	1.42	0.38	26.6	
VA	[L]	7.31	5.10	69.8	
TLC-SB	[L]	7.46	5.28	70.8	
FRC-SB	[L]	3.65	3.77	103.1	
RV-SB	[L]	2.34	2.88	123.1	
RV%TLC-SB	[%]	35.02	54.57	155.8	
Hb	[g/l]		148		
DLCOc SB	[mmol/min/kPa]	10.63	1.92	18.1	



Beurteilung:

Warum soll eine LVR bei COPD sinnvoll sein?

- Ueberblähung mit Abflachung und Dysfunktion des Zwerchfells / Interkostalmuskeln
- Kompression des Lungenparenchyms
- „Elastic Recoil“: natürlich elastische Retraktionskraft der Lunge
- Weniger dynamische Ueberblähung
- Bessere linksventrikuläre Füllung aufgrund vermindertem intrathorakalem Druck

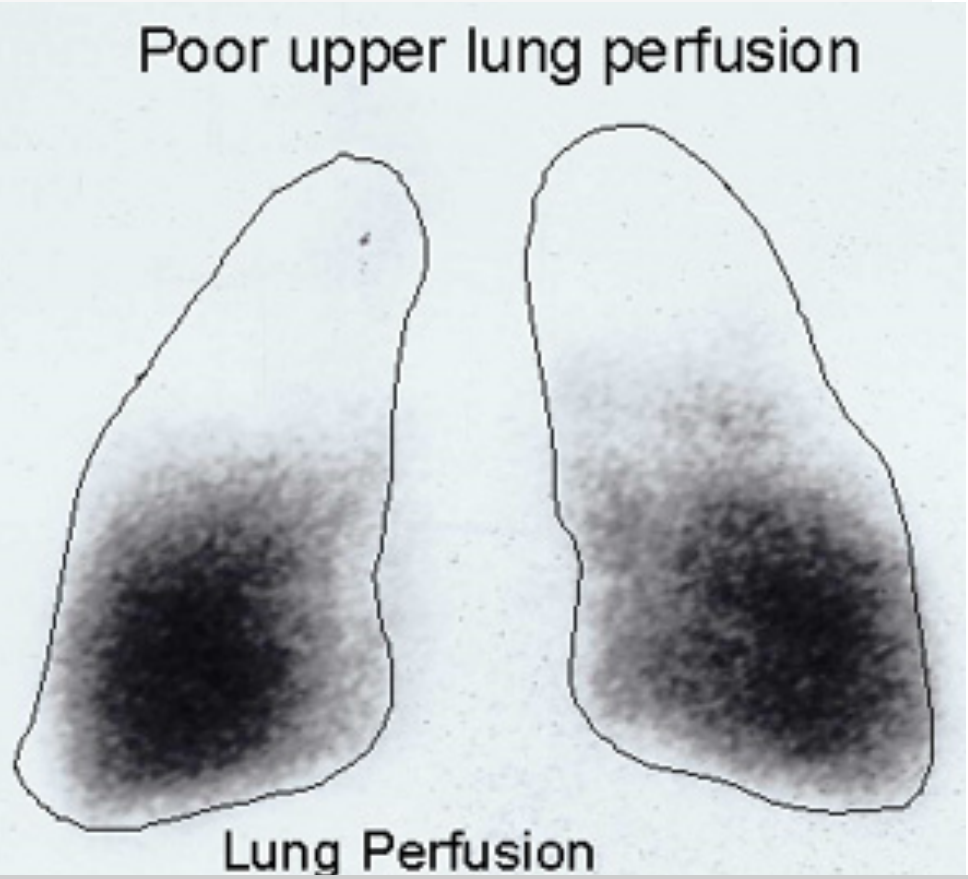
The NEW ENGLAND JOURNAL of MEDICINE

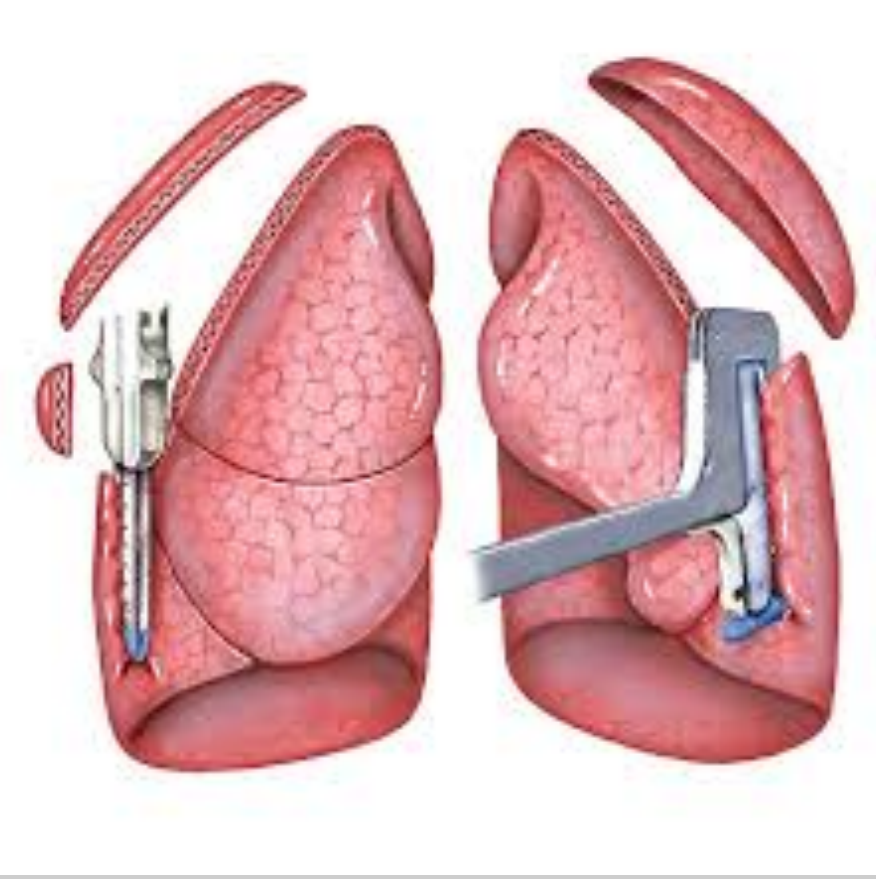
ESTABLISHED IN 1812 MAY 22, 2003 VOL. 348 NO. 21

A Randomized Trial Comparing Lung-Volume–Reduction Surgery with Medical Therapy for Severe Emphysema

National Emphysema Treatment Trial Research Group*

Lungenvolumenreduktionschirurgie



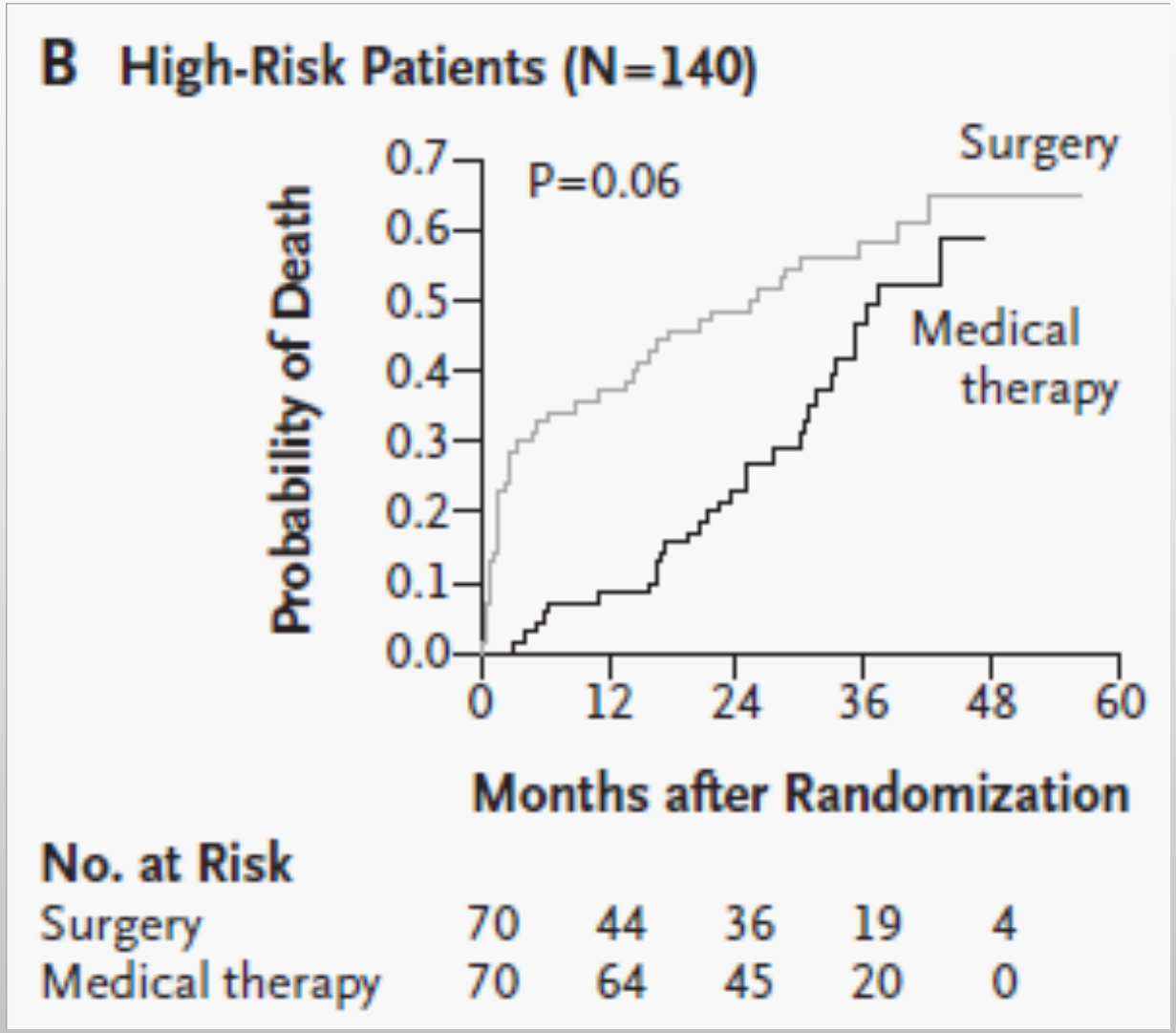


Ein- / Ausschlusskriterien

Parameter	Indications	Contraindications
Clinical	Age <75 years	Age ≥75 years
	Ex-smoker (>6 months)	Current smoking
	Clinical picture consistent with emphysema	Surgical constraints (eg, previous thoracic procedure, pleurodesis, chest wall deformity)
	Dyspnea despite maximal medical therapy and pulmonary rehabilitation	Pulmonary hypertension (PA systolic >45 mmHg, PA mean >35 mmHg)
Comorbid illness*		Clinically significant bronchiectasis
		Clinically significant coronary heart disease
		Heart failure with an ejection fraction <45 percent
		Uncontrolled hypertension
		Obesity¶
Physiology	FEV1 after bronchodilator <45 percent predicted	FEV1 ≤20 percent predicted with either DLCO ≤20 percent predicted or homogeneous emphysema
	Hyperinflation (TLC >100 percent predicted, RV >150 percent)	PaO2 ≤45 mmHg on room air
	Post rehabilitation 6-minute walk distance >140 meters	PaCO2 ≥60 mmHg
	Low post rehabilitation maximal achieved cycle ergometry watts$^{\Delta}$	
Imaging	Chest radiograph - hyperinflation	
	HRCT confirming severe emphysema, ideally with upper lobe predominance	Homogeneous emphysema with FEV1 ≤20 percent predicted
		Significant pleural or interstitial changes on HRCT
		Nonupper lobe predominant emphysema and high post rehabilitation maximal achieved cycle ergometry watts$^{\diamond}$

Hochrisikopopulation

- FEV1 < 20%
- DCO < 20%



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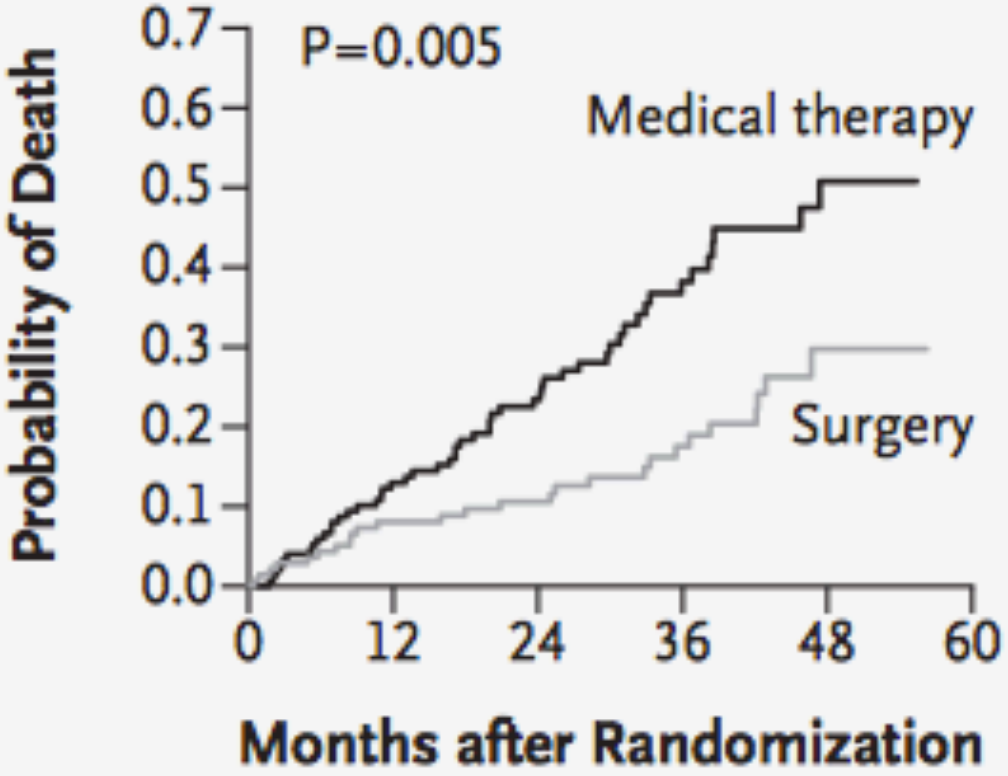
		Nonupper lobe predominant emphysema and high post rehabilitation maximal achieved cycle ergometry watts◊

Resultate: Ueberleben

oberlappenbetont, stark eingeschränkte körperliche Leistungsfähigkeit

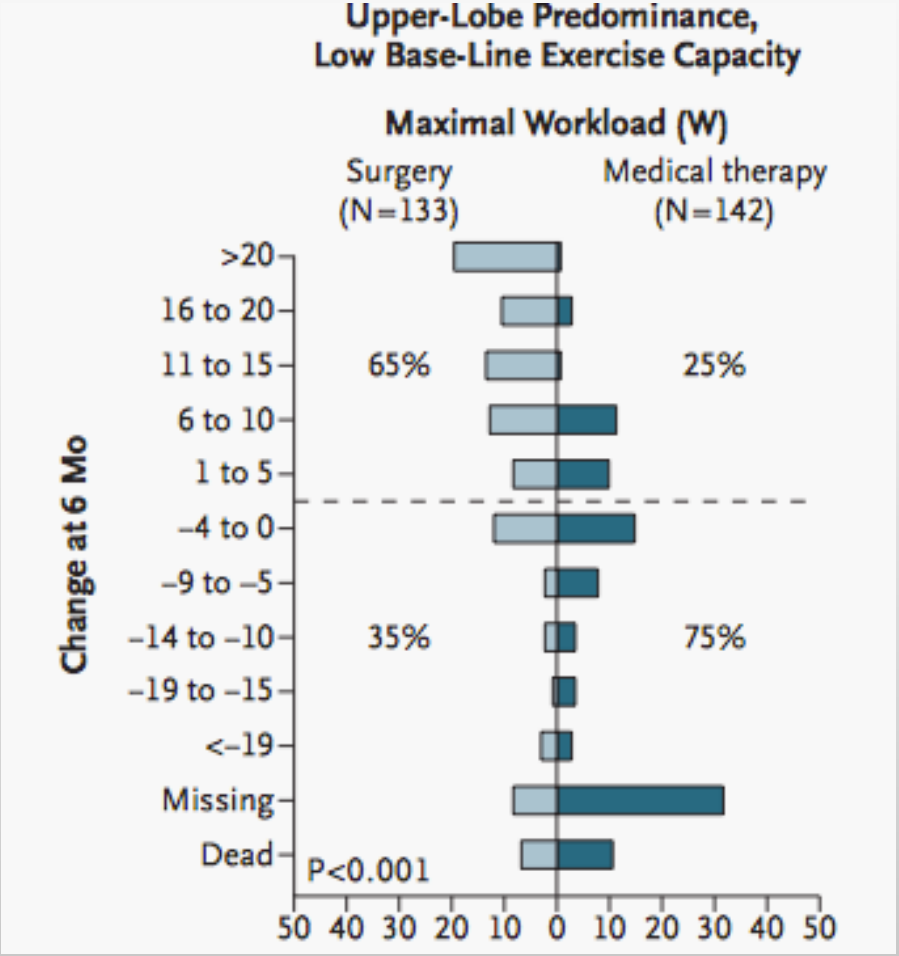


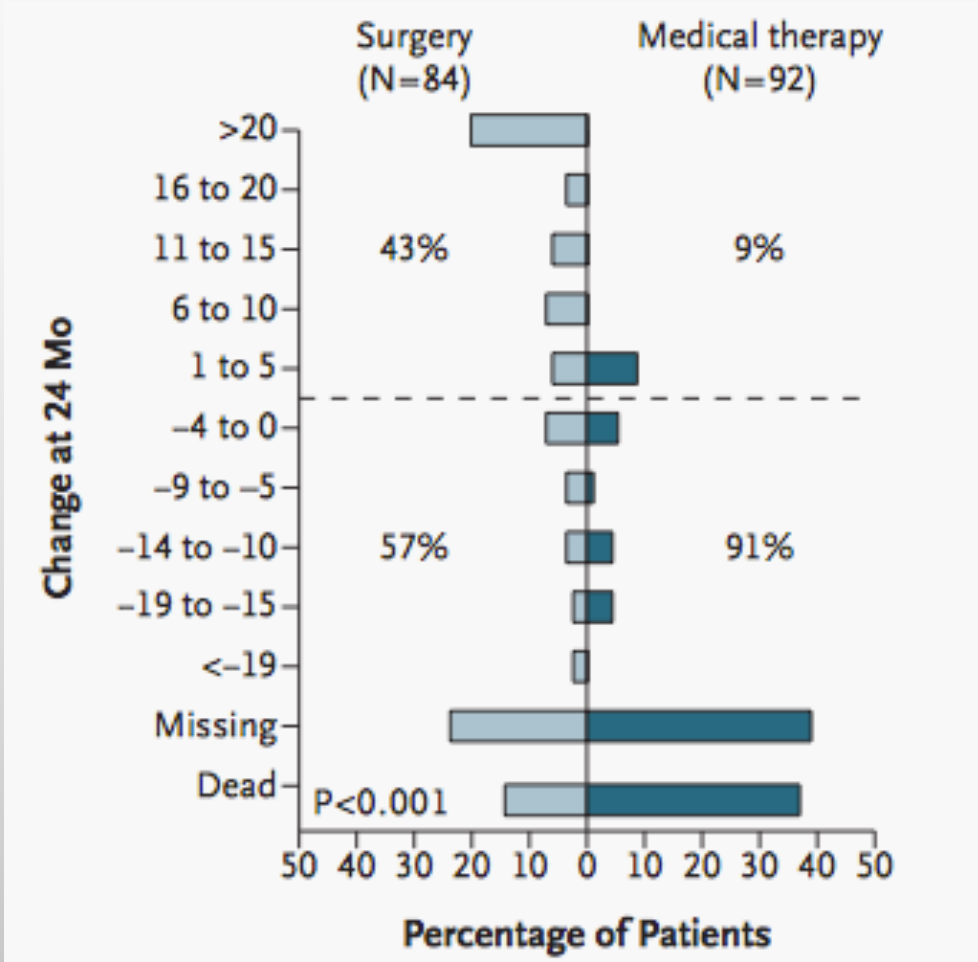
No. at Risk

Surgery	139	121	93	61	17
Medical therapy	151	120	85	43	13

NETT Trial. NEJM 2003.

Resultate: körperliche Leistungsfähigkeit oberlappenbetont, körperlich stark eingeschränkt





NETT Trial. NEJM 2003

Resultat nach LVRS

Therapie	Zeit nach Therapie (Monate)	Δ FEV_1, Liter (%)	Δ RV/TLC (%)	Δ MRC (%)	Δ 6-MWT, Meter (%)
LVRS***	6	+0,38 (49)*	−0,14 (21)*	−2,2 (63)*	+146 (60)*
	12	+0,27 (35)*	−0,12 (18)*	−2,0 (57)*	+142 (58)*

LVRS bei oberlappenbetontem Lungenemphysem

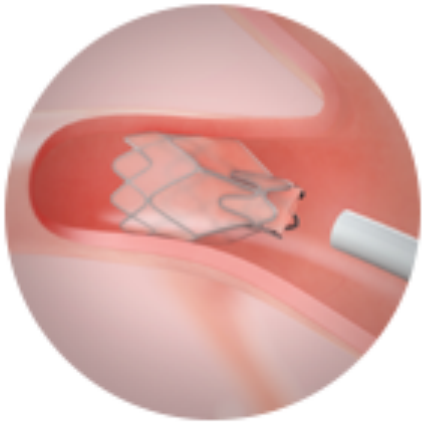
- Ueberleben
- Leistungsfähigkeit
- Lungenfunktion
- Weniger Exazerbation
- Dauer 3- 5 Jahre

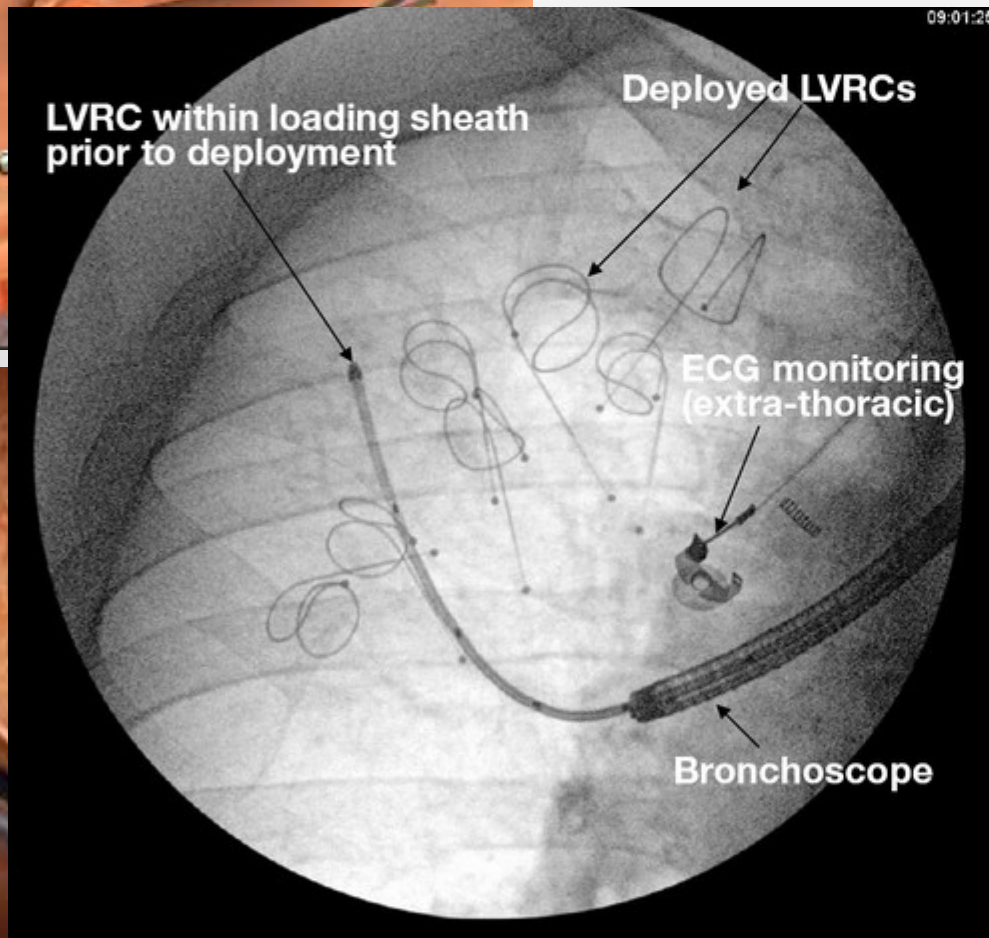
NETT Trial. NEJM 2003

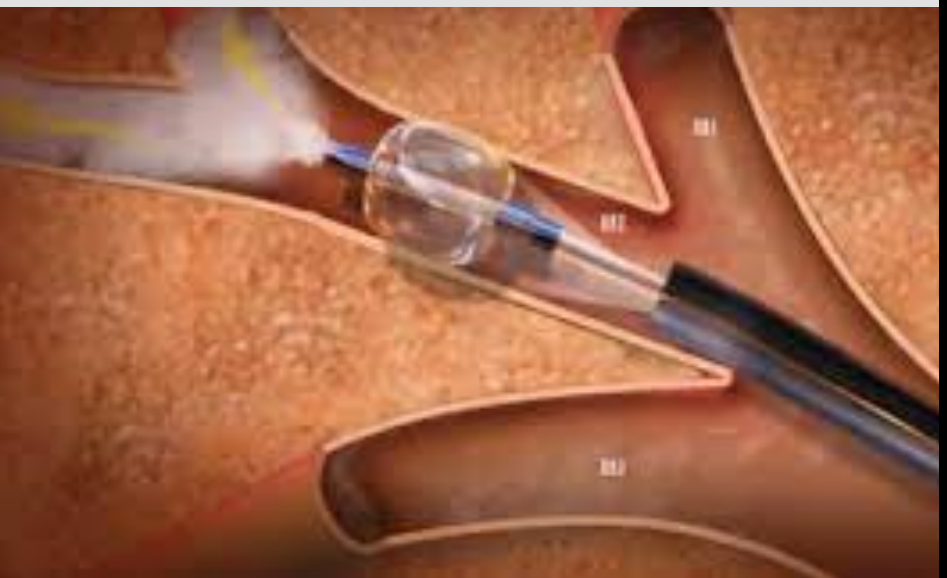
Komplikationen nach LVRS

- 30%
- Luftfisteln
- Respiratorische Insuffizienz
- Pneumonien
- Mortalität 5.5% nach 90 Tagen, USZ: 1%
- Mediane Hospitalisationszeit 12 Tage

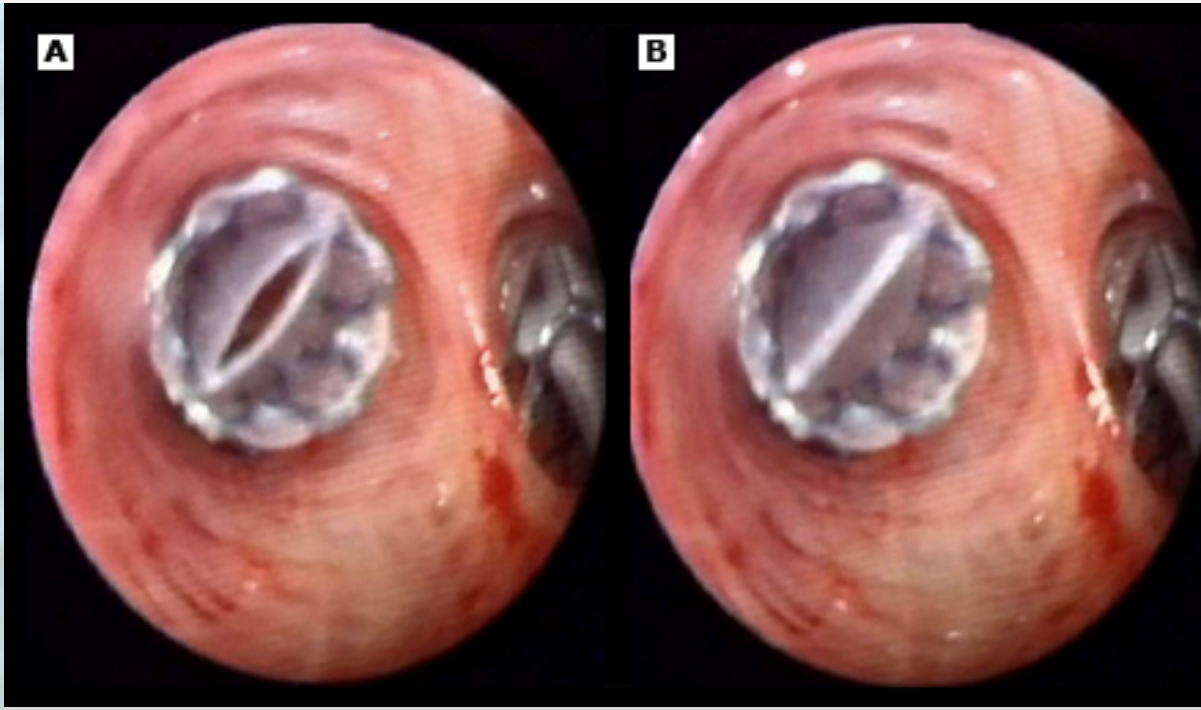
Bronchoskopische LVR







Bronchoskopische Verfahren
1. Ventile



Exspiration

Inspiration

Table 2. Primary and Secondary Efficacy Outcomes in the Intention-to-Treat Population (Change from Baseline at 6 Months).*

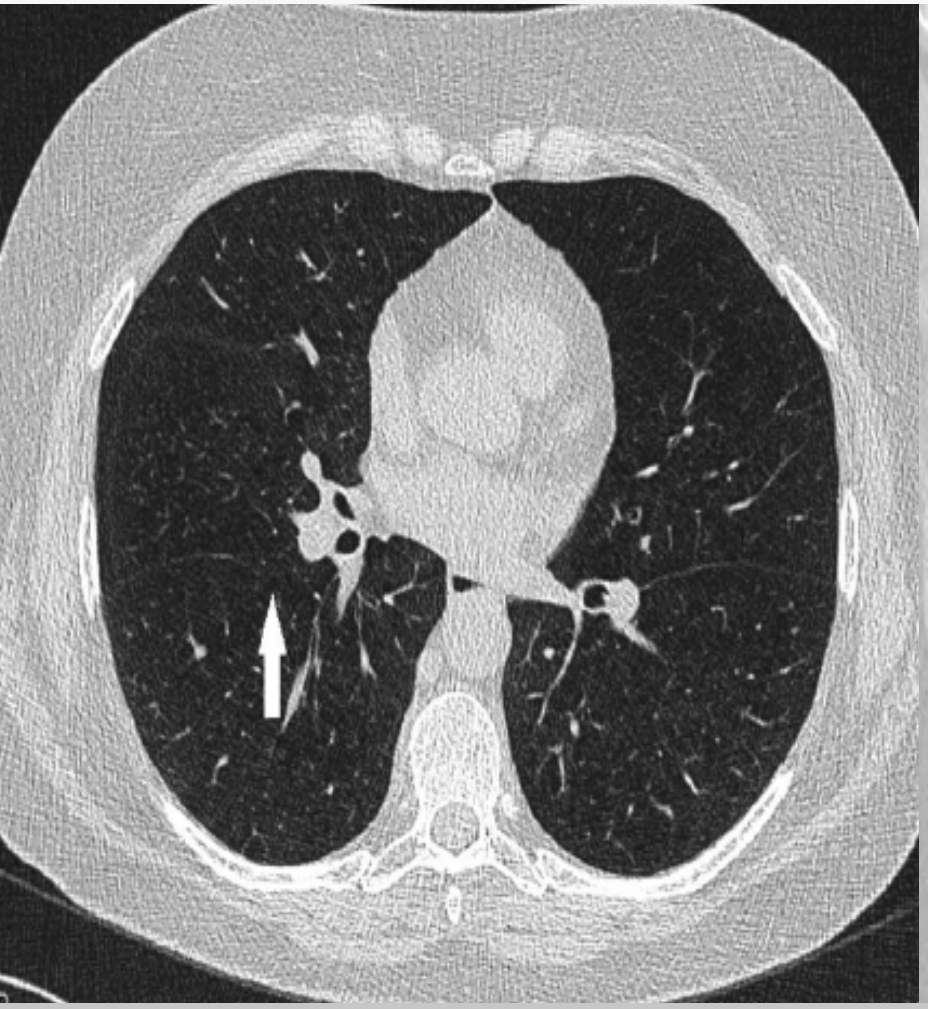
Outcome	Endobronchial-Valve Therapy (N=220)	Control (N=101)	Between-Group Difference in Change from Baseline	P Value
	number (95% confidence interval)			
Primary outcome				
FEV_1				
Mean absolute percent change from baseline	4.3 (1.4 to 7.2)	−2.5 (−5.4 to 0.4)	6.8 (2.1 to 11.5)	0.005
Mean change in value from baseline — ml	34.5 (10.8 to 58.3)	−25.4 (−48.3 to −2.6)	60.0 (21.5 to 98.4)	0.002
Mean absolute percent change in predicted value from baseline	1.0 (0.2 to 1.8)	−0.9 (−1.7 to −0.1)	1.9 (0.5 to 11.2)	0.007
Distance on 6-min walk test†				
Median absolute percent change from baseline	2.5 (−1.1 to 6.1)	−3.2 (−8.9 to 2.4)	5.8 (0.5 to 11.2)	0.04
Median change from baseline — m	9.3 (−0.5 to 19.1)	−10.7 (−29.6 to 8.1)	19.1 (1.3 to 36.8)	0.02
Secondary outcome				
Mean change in score on SGRQ from baseline‡	−2.8 (−4.7 to −1.0)	0.6 (−1.8 to 3.0)	−3.4 (−6.7 to 0.2)	0.04
Mean change in score on Modified Medical Research Council dyspnea scale from baseline§	−0.1 (−0.21 to 0.09)	0.2 (0.01 to 0.37)	−0.3 (−0.50 to −0.01)	0.04
Mean change in cycle ergometry peak workload from baseline — W	0.6 (−1.5 to 2.7)	−3.2 (−4.5 to −1.9)	3.8 (0.1 to 7.5)	0.05
Median change in supplemental oxygen use from baseline — liters/day†	0.0 (−117.3 to 117.3)	0.0 (−148.2 to 148.2)	−12.0 (−76.7 to 52.7)	0.005

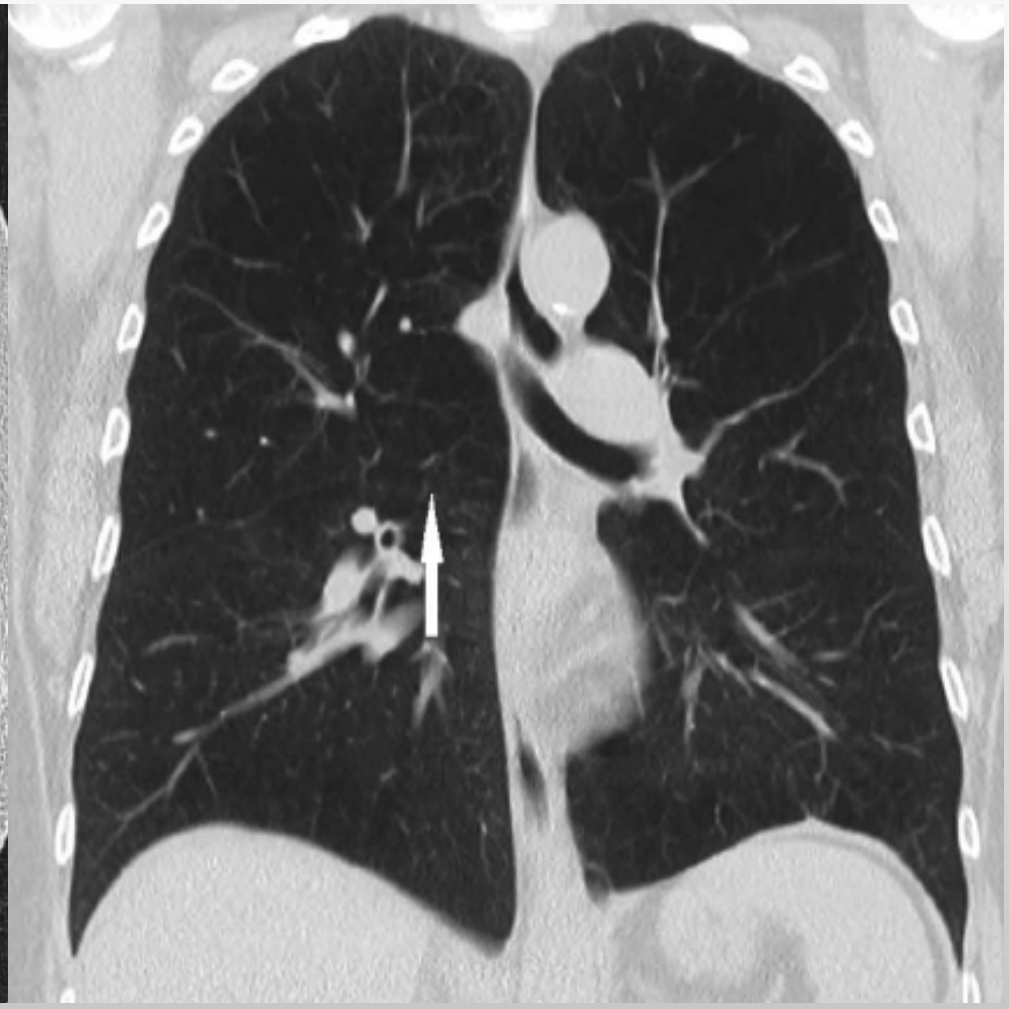
Sciurba et al. A randomized study of endobronchial valves for advanced emphysema. NEJM 2010.

Heterogenität/ Fissuren

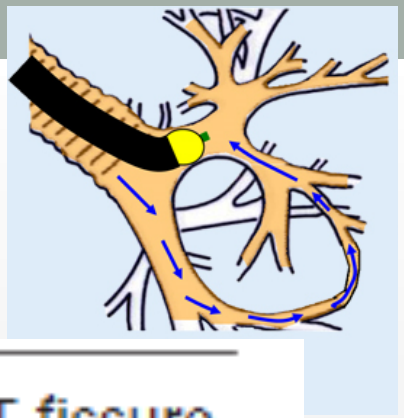
Subgroup and Outcome	Percent Change from Baseline at 6 Mo		Percent Change from Baseline at 12 Mo	
	Difference between EBV Group and Control Group	P Value†	Difference between EBV Group and Control Group	P Value†
	% (95% CI)		% (95% CI)	
High heterogeneity				
FEV_1	10.7 (3.5 to 17.9)	0.004	13.3 (5.7 to 20.9)	<0.001
Distance on 6-min walk test	12.4 (4.8 to 20.1)	0.002	7.1 (−0.8 to 14.9)	0.08
Low heterogeneity				
FEV_1	2.5 (−3.1 to 8.2)	0.38	1.5 (−4.7 to 7.6)	0.64
Distance on 6-min walk test	−1.0 (−6.4 to 8.4)	0.80	−0.6 (−6.4 to 7.7)	0.84
Complete fissure				
FEV_1	16.2 (8.8 to 23.8)	<0.001	17.9 (9.8 to 25.9)	<0.001
Distance on 6-min walk test	7.7 (−1.8 to 17.2)	0.14	3.9 (−4.0 to 11.8)	0.31
Incomplete fissure				
FEV_1	2.0 (−3.9 to 7.9)	0.51	2.8 (−3.8 to 9.4)	0.41
Distance on 6-min walk test	5.3 (−1.5 to 12.2)	0.13	4.5 (−2.7 to 11.8)	0.20

Inkomplette Fissuren → Kollateralventilation





Kollateralventilation



	Chartis System	HRCT fissure
Accuracy (%)	74	77
Sensitivity [true positive rate] (%)	86.1 (70.5, 95.3)	75.0 (57.8, 87.9)
Specificity [true negative rate] (%)	60.6 (42.1, 77.1)	78.8 (61.1, 91.0)
Positive predictive value (%)	70.5	79.4
Negative predictive value (%)	80.0	74.3

HRCT, high-resolution computerized tomography.

Resultate

	FEV1 nach 3 - 6 Monaten	RV, RV/TLC		6 Min. Gehtest
1)	+0.22 (25%)*	-800ml (14%)*		+102m *
2)	+0.06 (8.77%)*	-260ml (3.95%)	*	+33*
3)	(22.7%) *	-831ml*		+106m*
4)	+0.24 L			+ 50m

Vorteil
Reversibel

* $p<0.05$

1) Venuta et al. Long-term Follow-up after bronchosccopic lung volume reduction in patients with emphysema. Eur Respir J 2012
2) Davey et al. Bronchoscopic lung volume reduction with endobronchial valves für patients with heterogeneous emphysema. «Believer Studie «
3) Endobrnochiale Valve Treatment versus standart medical care in Patients with Emphysema. J am Respir Crit Care med. 2015 «STELVIO»
4) Park et al. International Journal of COPD. 2015

Zahlen bronchoskopische LVR mittels Ventilimplantation

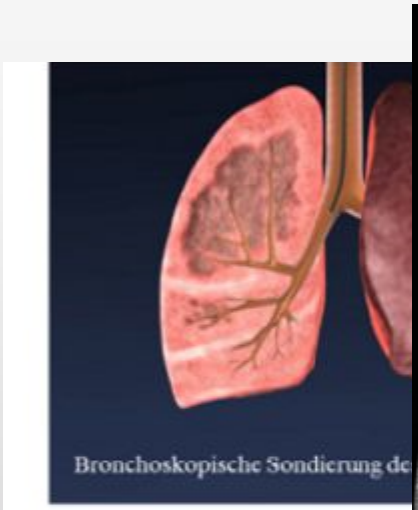
- Durchschnittliche Hospitalisationszeit 5 Tage

Table 1 Percentage of patients experiencing adverse events at 90 days in the randomised clinical trials

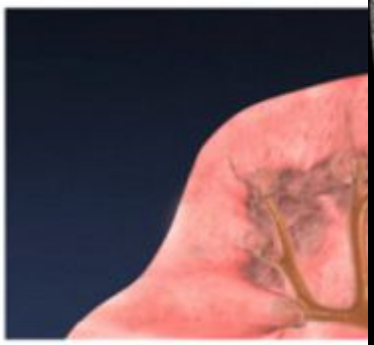
	Treatment	Control
Death	0.8	0.6
COPD exacerbation with hospitalisation	9.2	4.8
COPD exacerbation without hospitalisation	10.5	15.7
Infection	1.2	0
Respiratory failure	2.2	0.7
Pneumonia distal to valve	1.9	–
Pneumonia other lobe	2.8	2.0
Haemoptysis: massive	0.6	0
Pneumothorax: >7 days	2.2	0
Emphysema	0	0

Data derived from Sciurba *et al*[24] Herth *et al*[25] and Ninane *et al*.[26]
COPD, chronic obstructive pulmonary disease.

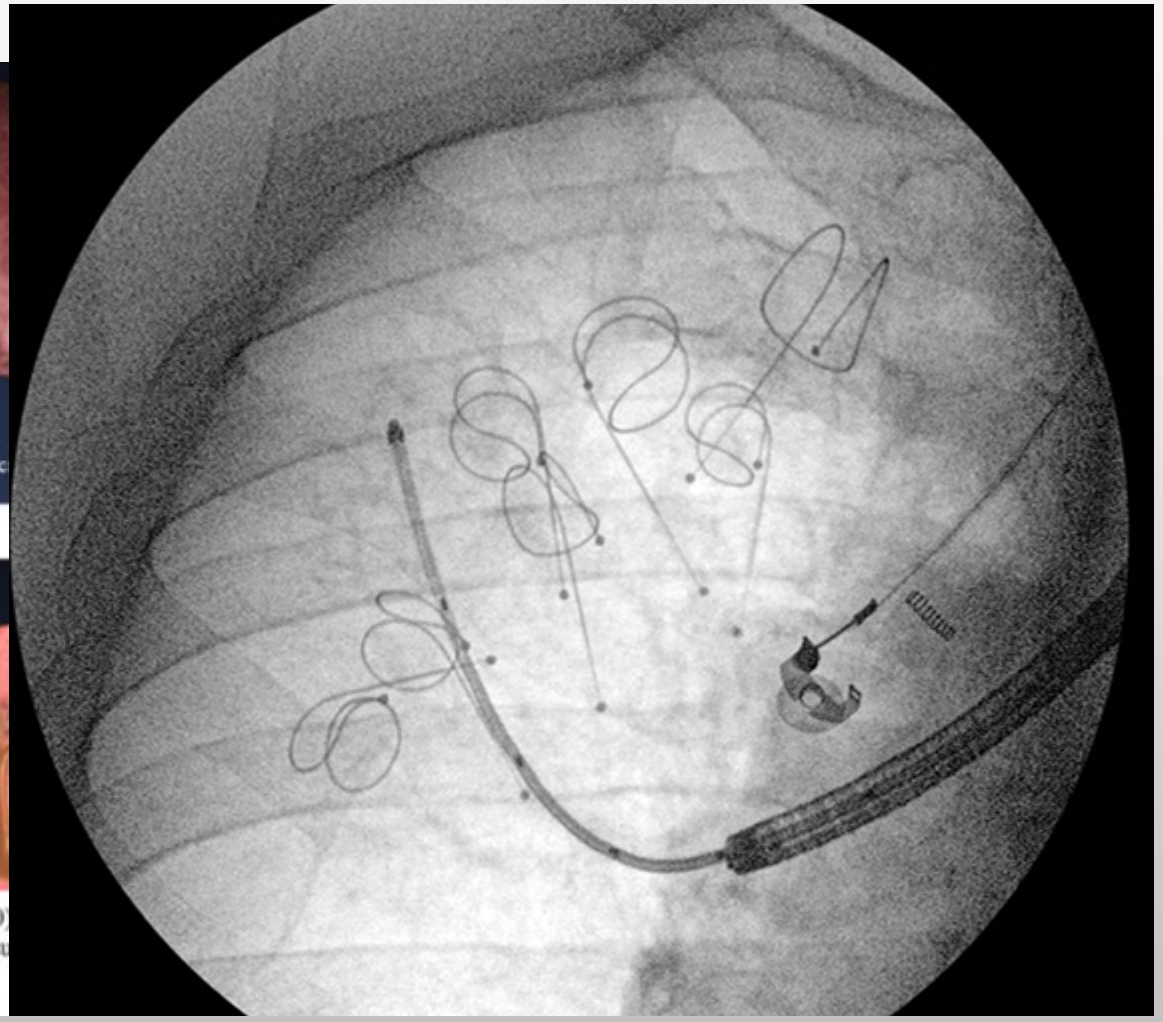
Bronchoskopische Verfahren
2 Coils



Bronchoskopische Sondierung de



Mehrere Coils sind platziert (∅ 10
ist reduziert. Atemluft kann in gesu
gelangen



Resultate Coils

	6 Months Overall group (N=58)	12 Months 12-month follow-up group (N=34)
FEV_1, L	+0.11±0.20 (n=54, p<0.001)	+0.11±0.30 (n=34, p=0.037)
FEV_1, % pred (% change)	+15.36±26.68 (n=54, p<0.001)	+16.04±35.54 (n=34, p=0.017)
FVC, L	+0.20±0.53 (n=54, p=0.008)	+0.28±0.45 (n=34, p=0.001)
RV, L	−0.65±0.90 (n=58, p<0.001)	−0.71±0.81 (n=34, p<0.001)
RV, % pred (% change)	−11.31±15.25 (n=58, p<0.001)	−13.75±12.65 (n=34, p<0.001)
RV/TLC	−4.51±12.19 (n=58, p=0.007)	−3.12±15.59 (n=34, p=0.245)
6MWD, m	+29.7±74.1 (n=56, p=0.004)	+51.4±76.1 (n=32, p=0.003)
SGRQ, points	−12.1±12.9 (n=56, p<0.001)	−11.1±13.3 (n=32, p<0.001)
mMRC, points	−0.6±1.2 (n=58, p<0.001)	−0.7±0.8 (n=34, p<0.001)

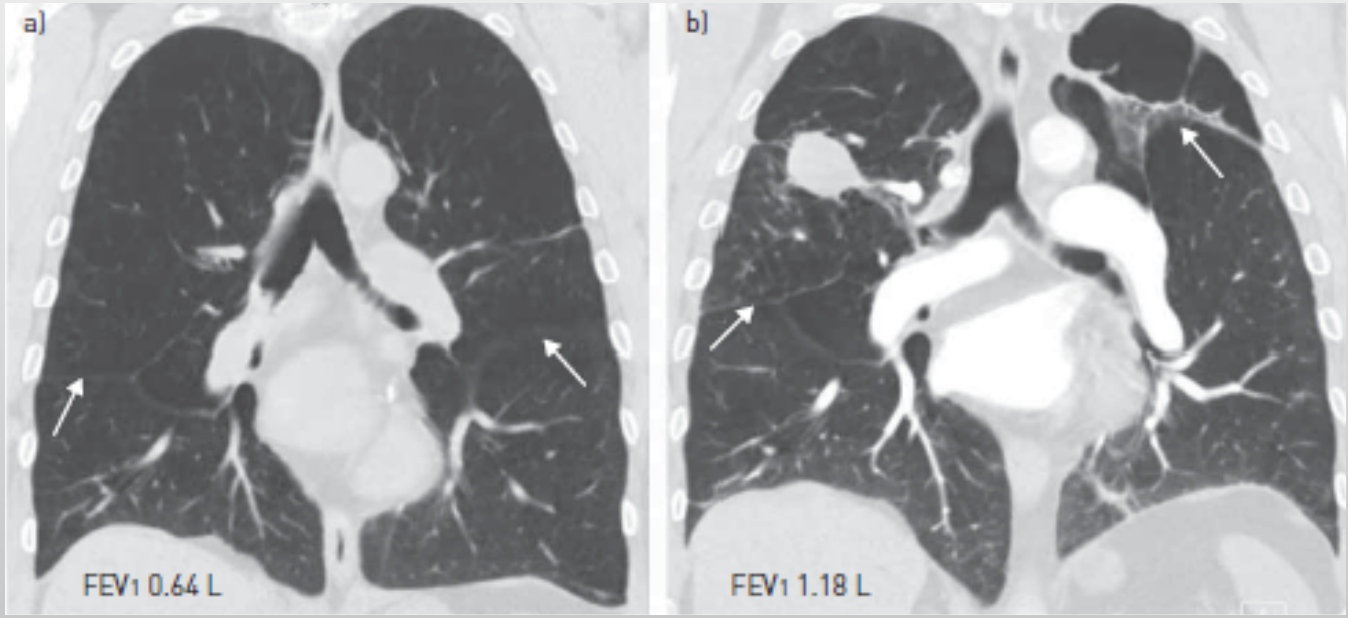
Deslee et al. Lung volume reduction coil treatment for patients with severe emphysema: a European Multicenter Trial. Thorax 2014

Nebenwirkungen Coils

	Treatment–1 month		>1–6 months		>6–12 months	
	Events	Patients	Events	Patients	Events	Patients
Serious respiratory adverse events						
COPD exacerbation	7	7	12	10	4	3
Pneumonia	6	5	3	3	6	6
Haemoptysis	1	1	0	0	0	0
Pneumothorax	4	4	2	2	1	1
Respiratory adverse events						
COPD exacerbation	8	7	21	15	19	15
Pneumonia	5	3	4	3	3	3
Mild haemoptysis (<5 mL)	61	35	3	3	2	2
Cough	2	2	3	3	0	0
Transient chest pain	28	20	7	6	3	3

Thermische/ chemische LVR

- Wasserdampf
- Polymerisierende Flüssigkeit: akutell nicht mehr durchgeführt



Zusammenfassung

Tabelle 2: Lungenfunktion, 6-Minuten-Gehdistanz und Dyspnoe nach chirurgischer und interventioneller Behandlung des Lungenemphysems** (modifiziert nach [3, 16, 18, 20, 23, 24]).

Therapie	Zeit nach Therapie (Monate)	Δ FEV_1, Liter (%)	Δ RV/TLC (%)	Δ MRC (%)	Δ 6-MWT, Meter (%)
LVRS***	6	+0,38 (49)*	−0,14 (21)*	−2,2 (63)*	+146 (60)*
	12	+0,27 (35)*	−0,12 (18)*	−2,0 (57)*	+142 (58)*
EBV****	6	+0,22 (25)*	−0,10 (14)*	−1,7 (44)*	+102 (36)*
	12	+0,21 (24)*	−0,10 (14)*	−1,5 (38)*	+63 (22)*
LVRC	6	+0,11 (13)*	−0,05 (6)*	−0,6 (20)*	+30 (9)*
	12	+0,11 (13)*	−0,03 (9)	−0,7 (23)*	+51 (16)*
Dampf	6	+0,14 (17)*	−0,03 (4)*	−0,9 (33)*	+46 (17)*
	12	+0,09 (10)*	−0,04 (5)	−0,8 (28)	+18 (6)
Schaum	6	+0,33 (31)*	−0,07 (11)*	−0	+12
	12	+0,28 (25)*	−0,10 (16)*	−1,0*	+9

* p <0,05 (Vergleich zu den präoperativen bzw. präinterventionellen Werten).
** Alle Werte entsprechen absoluten (relativen) Änderungen der Medianwerte im Vergleich zu den präoperativen bzw. präinterventionellen Werten.
*** Ausschliesslich heterogene Emphyseme.
**** Ausschliesslich heterogene Emphyseme, jedoch unabhängig von der Fissurintegrität bzw. Kollateralventilation.
LVRS = Lungenvolumenreduktionsoperation; LVRC = Lungenvolumenreduktions-Coil; EBV = endobronchiale Ventile; FEV_1 = forciertes exspiratorisches Volumen in einer Sekunde; RV/TLC = Residualvolumen/totale Lungenkapazität; MRC = Dyspnoe-Skala des Medical Research Councils; 6-MWT = 6-minute walk test (6-Minuten-Gehtest).

Zahlen entnommen aus SMF 2015.

Zusammenfassung: Basics first!

Inhalative Therapie* der COPD[1,2]

Therapieempfehlung Patientengruppe A (tiefes Risiko, wenig Symptome)	
Erste Wahl	**Alternative**
SAMA oder **SABA**	**LAMA** oder **LABA** oder **SAMA + SABA**

Therapieempfehlung Patientengruppe B (tiefes Risiko, viele Symptome)	
Erste Wahl	**Alternative**
LAMA oder **LABA**	**LAMA + LABA**

Therapieempfehlung Patientengruppe C (hohes Risiko, wenig Symptome)	
Erste Wahl	**Alternative**
0-1 Exazerbationen pro Jahr	
LAMA	**LAMA + LABA**
≥2 Exazerbationen pro Jahr	
ICS + LABA	

Therapieempfehlung Patientengruppe D (hohes Risiko, viele Symptome)	
Erste Wahl	**Alternative**
0-1 Exazerbationen pro Jahr	
LAMA	**LAMA + LABA**
≥2 Exazerbationen pro Jahr	
ICS + LABA oder **ICS + LABA + LAMA**	**LAMA + LABA + ICS**

Nicht-medikamentöse Therapie: Rauchstopp, Grippeimpfung, körperliche Aktivität, Patientenschulung

SAMA	Kurzwirksames Anticholinergikum	LABA	Langwirksamer $ß_2$-Agonist, z.B. Onbrez® Breezhaler®
SABA	Kurzwirksamer $ß_2$-Agonist	LAMA + LABA	Duale Bronchodilatation, z.B. Ultibro® Breezhaler®
LAMA	Langwirksames Anticholinergikum, z.B. Seebri® Breezhaler®	ICS	Inhalatives Steroid
		ICS + LABA	Inhalatives Steroid und langwirksamer $ß_2$-Agonist

*Für weitere Therapieempfehlungen wie z.B. PDE-4 Hemmer sind die GOLD-Empfehlungen zu konsultieren auf www.goldcopd.org.

COPD Gold III-IV

Lungenemphysem

- Alle pharmakologischen und nicht pharmakologischen Behandlungsmöglichkeiten (inkl. pulmonaler Rehabilitation) ausgeschöpft
- Sistierter Zigarettenkonsum

FEV_1 <50%, RV >180%, RV/TLC >60%, 6-MWT 150–400 m

- Computertomographie: Emphysemmorphologie?
- Lungenperfusionsszintigraphie: Zielzonen?

Heterogen		Homogen	
Keine Kollateralventilation; Intakte Interlobärfissuren	Kollateralventilation Inkomplette Fissuren		
▪ LVRS ▪ Ventile	▪ LVRS ▪ LVRC ▪ Dampf	▪ LVRS ▪ LVRC ▪ Ventile ▪ Dampf	▪ Alter <60–65 J. ▪ Bronchiektasen ▪ DLCO & FEV_1 <20% ▪ Pulmonale Hypertonie ▪ pO_2 <6,0 kPa ▪ pCO_2 >8,0 kPa **Lungentrans-plantation?**

Danke für die Aufmerksamkeit